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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/817,448	03/26/2001	H. Craig Dees	PHO-120	2388

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EXAMINER	
GABEL, GAILENE	
ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 12/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/817,448	DEES ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2004 and 27 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,11-14,16-33,36-40 and 46-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,11-14,16-33,36-40 and 46-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/27/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/21/04 has been entered.

Amendment Entry

2. Applicant's amendment and response filed 9/21/04 is acknowledged and has been entered. Claims 1-5, 11-14, 16, 17, 22, 27-29, 46, and 47 have been amended. Claims 6, 8-10, 15, and 34 have been cancelled. Applicant's response filed 9/27/04 is also acknowledged. Accordingly, claims 1-5, 11-14, 16-33, 36-40, and 46-50 are pending and are under examination.

Rejections Moot or Withdrawn

3. Rejections of claims 6, 8-10, 15, and 34 are now moot in light of Applicant's cancellation of the claims.

4. In light of Applicant's amendment, the rejections of claims under 35 U.S.C. 102(b) as being anticipated by Serafini et al. (Journal of Nuclear Medicine, 1975) and 35

U.S.C. 103(a) as being unpatentable over Serafini et al. (Journal of Nuclear Medicine, 1975), are being withdrawn.

5. In light of Applicant's amendment, the rejections of claims 1, 3, 5, 12, 16, 18, 20, 29, 31, 33, 36-39, 46-48, and 50 under 35 U.S.C. 102(b) as being anticipated by Neckers D. (Journal of Photochemistry and Photobiology, A: Chemistry (1989)) is being withdrawn.

6. In light of Applicant's amendment, the rejections of claims under 35 U.S.C. 102(b) as being anticipated by Fondren et al. (Environ Entomol (1978)) and 35 U.S.C. 103(a) as being unpatentable over Fondren et al. (Environ Entomol (1978)), are being withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 16-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 provides for the use of a halogenated xanthene, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 16-21 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

New Grounds of Rejection

New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-5, 11-14, 16-33, 36-40, and 46-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

In this case, the specification does not appear to provide literal or adequate descriptive support for the recitation of "(pharmaceutical composition ... consisting of) sodium or potassium salt of a halogenated xanthene ". Applicant points to Table 1 for support which provides tabulation of the different halogenated xanthene compounds and their different R^1 and R^2 substitutions which include therein sodium and potassium salts; however, it fails to provide adequate descriptive support for the recitation of

"(pharmaceutical composition ... consisting of) sodium or potassium salt of a halogenated xanthene." Some of the halogenated compounds enumerated in Table 1 do not even list sodium and potassium salts as being inclusive to the R^1 and R^2 substitutions. Additionally, page 13, line 22 to page 14, line 7 of Applicant's disclosure points out that positions R^1 and R^2 are functional derivatives used to optimally target and attach halogenated xanthenes to specific tissues or sites.

The specification also does not appear to provide literal or adequate descriptive support for the recitation of "said halogenated xanthene does not contain a radioisotope". This is a recitation of a negative limitation excluding radioisotope within the realm of the recited halogenated xanthene but the specification does not provide teaching or disclosure for the recitation of a negative limitation in the claims excluding a radioisotope. Specific guidance for the exclusion of a radioisotope is not taught, the recitation of the negative limitation, "does not contain a radioisotope" is therefore not supported or disclosed in the instant specification.

Since the limitations discussed supra lack antecedent basis in the specification, do not flow from the teaching of Applicant's disclosure, and none of the originally filed claims recited the above limitations in question, they are considered to constitute new matter. See In re ANDERSON, 176 USPQ 331 (CCPA 1973).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11

F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 22-28 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 41-45 of copending Application No. 10/331,854. Although the conflicting claims are not identical, they are not patentably distinct from each other because the conflicting claims are drawn to a method of treatment using a sodium or potassium salt of a halogenated xanthene as radiosensitizer or intracorporeal medicament applied into or proximate to diseased tissue and for subsequent activation by ionizing radiation.

ASN 10/331,854 differ from the instant invention in failing to recite that the ionizing radiation has an energy of greater than approximately 1 KeV.

However, it is maintained that the level of ionizing radiation emitted for the purpose of activation, i.e. energy greater than approximately 1 KeV, is a result effective variable which the prior art reference has shown may be altered in order to achieve optimum results. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation."

Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since Applicant has not disclosed that the specific limitation recited in claim 22 is for any particular purpose or solve any stated problem, and the prior art teaches that ionizing radiation emission may vary according to the tissue sample being treated, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable range of the method disclosed by ASN 10/331,854 by normal optimization procedures.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

10. Claims 22-28 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2, 4-15, 17, 18, 20, 22-26, 28, 30, and 32 of U.S. Patent No. 6,331,286. Although the conflicting claims are not identical, they are not patentably distinct from each other because the conflicting claims are drawn to a method of treatment using a sodium or potassium salt of a halogenated xanthene as radiosensitizer or intracorporeal medicament applied into or proximate to diseased tissue and for subsequent activation by ionizing radiation

US Patent 6,331,286 differ from the instant invention in failing to recite that the ionizing radiation has an energy of greater than approximately 1 KeV.

However, it is maintained that the level of ionizing radiation emitted for the purpose of activation, i.e. energy greater than approximately 1 KeV, is a result effective variable which the prior art reference has shown may be altered in order to achieve optimum results. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since Applicant has not disclosed that the specific limitation recited in claim 22 is for any particular purpose or solve any stated problem, and the prior art teaches that ionizing radiation emission may vary according to the tissue sample being treated, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable range of the method disclosed by US Patent 6,331,286 by normal optimization procedures.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The claimed invention is drawn to a medicament or a pharmaceutical composition consisting of sodium or potassium salts of a halogenated xanthene in a pharmaceutical delivery vehicle, which is used in combination with ionizing radiation, for treatment of human or animal diseased tissue. Accordingly,

11. Claims 1, 3, 5, 16, 18, 29, 31, 33, 36-38, 46, 47, and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by Johansson (Svensk Farmaceutisk Tidskrift (1973) 77 (13): 641-647 (Abstract).

Johansson teaches analysis and purification of Rose Bengal Sodium for use as reference substance and in pharmaceutical preparations (pharmaceutical delivery vehicle). According to Johansson, the Rose Bengal Sodium is sufficiently pure for the International Pharmacopeia, 1971. Johansson teaches a combination of recrystallization and iodination procedure to produce the compound. See Abstract.

12. Claims 1, 3, 5, 16, 18, 29, 31, 33, 36-38, 46, 47, and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by Crounse et al. (US Patent 4,647,578).

Crounse et al. disclose that soluble sodium or potassium salts of halogenated xanthene dyes include erythrosin B, phloxin B, and Rose Bengal and are known to have photodynamic activity. According to Crounse et al., these compounds have utility in foodstuffs and in pharmaceutical applications, i.e. with specific pharmaceutical delivery vehicle, because they are essentially non-toxic to mammals and are safe for human consumption or treatment (see columns 3 and 4). Crounse et al. incorporate the compounds into aqueous solutions and dispersions (see Abstract).

13. Claims 1-5, 11-14, 16-33, 36-40, 46-50 are rejected under 35 U.S.C. 102(b) as being anticipated Dees et al. (US Patent 6,331,286).

Dees et al. teach a pharmaceutical composition consisting of a sodium or potassium salt of halogenated xanthene in a pharmaceutical delivery vehicle for use in treatment of cancer and infectious disease by sensitization or activation or exposure with ionizing radiation. Dees et al. teach applying ionizing radiation having energy greater than approximately 1 KeV. See entire document.

14. Claims 1-5, 11-13, 16-21, 29-33, 36-40, 46-50 are rejected under 35 U.S.C. 102(b) as being anticipated by Heitz et al. (US Patent 4,846,789).

Heitz et al. disclose halogenated xanthene dyes, which are administered to warm blooded animals and incorporated into infected tissue for activation by electromagnetic radiation (see Abstract and Figure 5). According to Heitz et al., the halogenated xanthene dyes may absorb radiation at wavelengths outside of the visible spectrum

including near infrared, and near to far ultraviolet spectrum (see column 3, lines 40-44). Heitz et al. teach that fluorescein derivatives having one or more substituents in the 4, 5, 6, 7, 2', 4', 5', and 7' positions selected from the group consisting of F, Cl, Br, with xanthene dyes including erythrosin B, phloxin B, eosin, and Rose Bengal are especially important (see column 4, lines 12-31). These halogenated xanthene dyes are incorporated into pharmaceutical delivery vehicles such as capsules or pellets for oral administration.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 2, 12, 14, 20, 30, 39, and 48 are rejected under 35 U.S.C. 103(a) as being unpantentable over Johansson (Svensk Farmaceutisk Tidskrift (1973) 77 (13): 641-647 (Abstract) or Crounse et al. (US Patent 4,647,578) in view of Neckers D. (Journal of Photochemistry and Photobiology, A: Chemistry 47: 1-29 (1989)).

Johansson or Crounse et al. have been discussed. Johansson and Crounse et al. differ from the instant invention in failing to teach applying ionizing radiation such as X-ray upon halogenated xanthene.

Neckers teaches and describes halogenated xanthenes such as Rose Bengal or 2,4,5,7- tetraiodo-3', 4', 5', 6'- tetrachlorofluorescein. Neckers specifically teach that Rose Bengal and Eosin have distinct spectral, photochemical, and photophysical properties. Neckers teaches that Rose Bengal, disodium salt is characterized 1) as a photodynamic sensitizer, 2) by large absorption in all solvents, 3) by its capacity to be activated as an imaging agent, with X-ray, 4) by a triplet that is completely quenched by oxygen, 5) by its concentration on selected tissues, i.e. tumor: its spectrum is most diagnostic of its immediate environment, 6) by bleaching in protic, polar solvents, (7) by its singlet quenched by strong oxidizing agents (see page 1). The absorption and emission spectra of certain Rose Bengal derivatives are enumerated in Table 2 and 3, respectively.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to apply X-radiation as taught by Neckers upon halogenated xanthenes as taught by Johansson and Crounse in order to effect activation of the compound

because Neckers specifically taught that halogenated xanthenes can be activated by X-ray as imaging agents.

Johansson, Crounse et al., and Neckers differ from the instant invention in failing to disclose the concentration of halogenated xanthene as greater than about 0.001% to less than about 20%. Johansson, Crounse et al., and Neckers also differ from the instant invention in failing teach applying ionizing radiation having an energy less than approximately 1000 MeV.

However, the concentration of halogenated xanthene in relation to the aqueous mixtures of the compound (claims 2 and 30) and the level of ionizing radiation applied thereto (claim 14), constitute result effective variables which have been shown may be altered depending on how xanthene is used or the tissue being treated in order to achieve optimum results. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since Applicant has not disclosed that the concentration range recited in instant claims 2, 14 and 30 are for any particular purpose or solve any stated problem

and prior art has shown that concentrations often vary according to use and purpose of the compound, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the active ingredient concentrations disclosed by the prior art by normal optimization procedures.

16. Claim 11, 13, 17, 21, 39, 40, and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johansson (Svensk Farmaceutisk Tidskrift (1973) 77 (13): 641-647 (Abstract) or Crounse et al. (US Patent 4,647,578) in view of Neckers D. (Journal of Photochemistry and Photobiology, A: Chemistry 47: 1-29 (1989) and in further view of Khaw et al. (US 5,780,052).

Johansson or Crounse et al. and Neckers have been discussed supra. Johansson, Crounse et al., and Neckers differ from the instant invention in failing to teach targeting the sodium and potassium salts of halogenated xanthenes in pharmaceutical delivery vehicle towards specific localized tissues. Johansson, Crounse et al., and Neckers also differ from the instant invention in failing to teach that the ionizing radiation is gamma radiation.

Khaw et al. disclose a method of enhancing effects of therapy that kills cancerous or infected cells in vivo by providing (immuno)liposomes specific for an internal cellular antigen present in degenerating neoplastic cells. Techniques are known for liposome targeting such as conjugating antibodies to cell-surface (malignant) antigens to pharmacologically active agents and labels to permit diagnosis, localization, and therapy toward tumors (see column 7, line 48 to column 8, line 3). The liposomes

contain antineoplastic agent for initiating therapy in a mammal to kill malignant cells in vivo (see column 2, last paragraph). The antineoplastic agents include radiosensitizing agents, cytotoxic agents, and radionuclides (see column 3, first paragraph and column 4, lines 18-27). In diagnostic procedures, (immuno)liposomes containing radiosensitizer and diagnostic agent which are specific for intracellular antigens, such as an imaging agent, are injected into a patient receiving radiation therapy. Following administration, an imaging technique is employed using computed axial tomography (CAT) scan, X-ray imaging, including gamma ray imaging. (See column 16, line 18 to column 17, lines 3).

It would have been obvious to one of ordinary skill in the art at the time of the invention to target pharmaceutical compositions consisting of sodium or potassium salts of halogenated xanthenes as taught by Johansson or Crounse as modified by Neckers into specific tissues as in the method taught by Khaw because Khaw specifically taught incorporating pharmaceutically of therapeutically activatable agents into liposomes or other delivery systems, for targeting delivery to specific tissue, ie. tumors, which allows for localization of the agent into the targeted tissue and sodium or potassium salts of halogenated xanthenes have been taught by Johansson or Crounse and Neckers to be activatable by radiation. Further, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to substitute use of gamma imaging as taught by Khaw into the teachings of Johansson or Crounse as modified by Neckers because use of gamma radiation is an obvious variation of imaging technique which is routinely known in the art.

17. Claims 14 and 22-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heitz et al. (US Patent 4,846,789).

Heitz et al. has been discussed supra. Heitz et al. differ from the instant invention in failing to teach applying ionizing radiation having an energy less than approximately 1000 MeV (claim 14) or alternatively, greater than approximately 1 KeV (claim 22).

However, different levels of ionizing radiation applied upon different halogenated xanthene dyes, constitute result effective variables which have been shown may be altered depending on how xanthene is used or the tissue being treated in order to achieve optimum results. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since Applicant has not disclosed that the values recited in instant claims 14 and 22 are for any particular purpose or solve any stated problem and prior art has shown that concentrations often vary according to use and purpose of the compound, absent unexpected results, it would have been obvious for one of ordinary

skill to discover the optimum workable ranges of the ionizing radiation levels disclosed by the prior art by normal optimization procedures.

Response to Arguments

18. Applicant's arguments filed 9/21/04 and 9/27/04 have been considered but are moot in view of the new grounds of rejection.

18. No claims are allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (571) 272-0820. The examiner can normally be reached on Monday, Tuesday, and Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gailene R. Gabel
Patent Examiner
Art Unit 1641
November 18, 2004

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641
11/22/04